Serial No. 10/045,884 Atty. Docket No. LcA 34 992

If there are any further fees due in connection with the filing of the present amendment, please charge the fees to undersigned's Deposit Account No. 13-3372.

Respectfully submitted,

Susan M. Pellegrino

June 3, 2003

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Specification (Attorney Docket No. LeA 34 992)

1) On page 15 of the specification, please replace the paragraph (lines 16-24) with the following paragraph:

C1

68 g (0.6 mol) of methanesulphonyl chloride are added dropwise at room temperature to 114g (0.51 mol) of the compound from Example 7 in 95g of pyridine. After stirring at room temperature for 18 hours, the mixture is diluted with 700 ml of water and extracted with dichloromethane. Filtration through silica gel and concentration afford 150 g of crude product, which is purified by crystallization from 1.5 l of cyclohexane/toluene mixture 3:1. The mother liquor is recrystallized from cyclohexane after concentration. 112 g of title compound are thus obtained as a colourless solid, m.p. 77-78°C.

$\exists_{589}^{20}$ $[\alpha]^{20}_{589}$ = -56.2 [c=0.9, CH_3OH]

2) On page 16 of the specification, please replace the paragraph (lines 7-14) with the following paragraph:

C2

112 g (0.37 mol) of the compound from Example 8, 200 g (1.87 mol) of benzylamine and 3.0 g (0.02 mol) of sodium iodide are heated at 100°C for 5 hours. After cooling, the solid is separated off and the organic phase is washed 2x with 2.5 l of water each time. The residual oil is taken up with 1 l of ethyl acetate. Washing the ethyl acetate phase with water and saturated sodium chloride solution and subsequent drying and concentration afford 114.5 g (quant.) of the title compound (HPLC purity: 93%) as an oil which is employed in the next stage.

$\exists_{589}^{20}$ $[\alpha]^{20}_{589}$ = -104 [c=0.5, CH_3OH]

3) On page 17 of the specification, please replace the paragraph (lines 10-22) with the following paragraph:

C3

114 g (0.37 mol) of the compound from Example 9 and 13.5 g (0.45 mol) of paraformaldehyde in 1 l of dioxane are treated with 4 g of copper(II) acetate and warmed to 50°C. 81 g (0.37 mol) of propargylsaccharin are added at this temperature. After stirring at 80°C for 2 hours, the mixture is concentrated and the residue is partitioned between toluene/water with addition of tonsil. After filtration of the mixture through Celite®, the organic phase is separated off and purified by flash chromatography on silica gel (toluene/ethyl acetate 10:1). Precipitation of the hydrochloride from ether using ethereal hydrochloric acid affords 226 g of crude product. After liberation of the free base using sodium hydrogencarbonate, this product is purified by chromatography on silica gel

C3 cont'd

(elution with toluene/ethyl acetate 20:1). The product fractions are treated with ethereal hydrochloric acid. 139 g (65%) of title compound are thus obtained as a solid, m.p. 106-109°C.

$\exists_{289}^{20}$ $[\alpha]^{20}_{289}$ = - 64.1 [c=0.8, CH_3OH]

4) On page 18 of the specification, please replace the paragraph (lines 9-19) with the following paragraph:

C4

120 g (0.21 mmol) of the compound from Example 10 in in 1.4 l of methanol are treated with 400 ml of conc. hydrochloric acid and 20 g of 10% palladium on active carbon. After hydrogenating at normal pressure and 20°C for 4 hours, the catalyst is filtered off and the filtrate is concentrated. The residue is concentrated 2x with toluene and dissolved using 400 ml of ethyl acetate. Addition of 800 ml of diethyl ether and stirring at room temperature for 18 h afford 90.5 g of solid after filtering off with suction and drying in vacuo. Recrystallization from 1 l of acetonitrile and washing the crystals with diethyl ether afford 70.8 g (69%) of title compound as colourless crystals, m.p. 153-154°C.

$\exists_{289}^{20}$ $[\alpha]^{20}_{289}$ = -65.9 [c=0.6, CH_3OH]

Claims (Attorney Docket No. L A 34 992)

C5

1. (Currently amended) A method of treating Parkinson's disease comprising administering to a subject in need thereof an effective amount of 2-[4-({[(2R)-8-isopropoxy-chroman-2-yl]methyl}-amino)butyl]-1,2-benzisothiazol-3(2H)-one 1,1-dioxide, its physiologically acceptable salts, hydrates or solvates.

2. (Previously amended) The method of claim 1 comprising administering an effective amount of 2-[4-({[(2R)-8-isopropoxy-chroman-2-yl]methyl}amino)butyl]-1,2-benzisothiazol-3(2H)-one 1,1-dioxide hydrochloride.

3. Cancelled.

4. Cancelled.

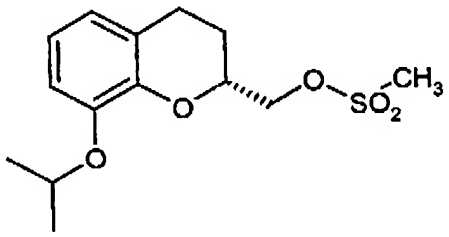
24 hours. After cooling, it is partitioned between toluene/water and filtered through Celite®. The organic phase is dried (magnesium sulphate) and concentrated. After flash chromatogrpahy (silica gel; elution with toluene/ethyl acetate gradients 3:1 – 2:1), 7 g of crude product are obtained, which is purified by chromatography on silica gel (gradient toluene/ethyl acetate 1:0 - 8:1). Yield: 2.9 g (52%) of oil.

R_F (silica gel, toluene/ethyl acetate 1:1): 0.4

$[\alpha]^{20}_{289} = -85$ [c = 0.5; $CHCl_3$]

Example 8

(R)-8-Isopropoxy-2-mesyloxymethyl-chroman



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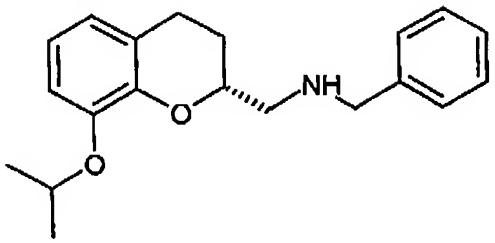
$[\alpha]^{20}_{289} = -56.2$ [c=0.9, CH_3OH] .

Example 9

(R)-2-Benzylaminomethyl-8-isopropoxy-chroman



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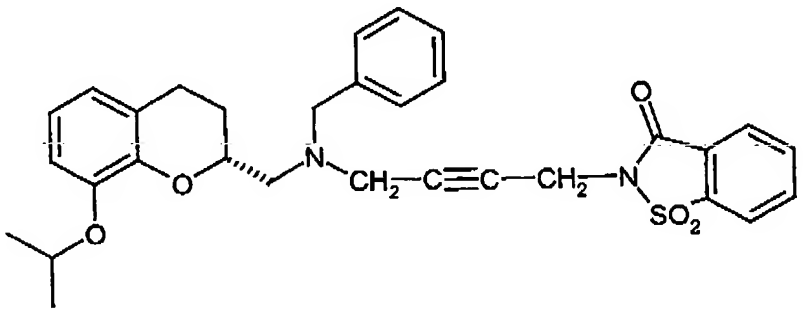
$[\alpha]^{20}_{289} = -104$ [c=0.5, CH_3OH]

Example10

(R)-2-(N-Benzyl-N-(4-(1,1-dioxido-3-oxo-2,3-dihydro-benzisothiazol-2-yl)-2-butinyl)-aminomethyl)-8-isopropoxy-chroman hydrochloride



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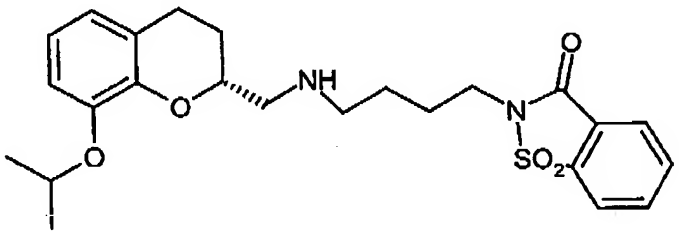
$[\alpha]^{20}_{289} = -64.1$ [c=0.8, CH_3OH]

Example 11

2-[4-({[(2R)-8-Isopropoxy-chroman-2-yl]methyl}amino)butyl]-1,2-benzisothiazol-3(2H)-one 1,1-dioxide has the following structure:



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$[\alpha]^{20}_{289}$ = -65.9 [c=0.6, CH_3OH]

Elemental analysis: $C_{24}H_{30}N_2O_5S \times HCl$

calc.:	C: 58.2	H: 6.3	N: 5.7	O: 16.2	Cl: 7.2 S: 6.5
found:	C: 58.0	H: 6.3	N: 5.7	O: 16.2	Cl: 7.1 S: 6.3